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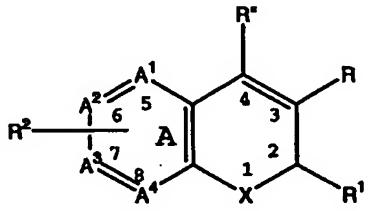
(54) Title: SUBSTITUTED BENZOPYRAN DERIVATIVES FOR THE TREATMENT OF INFLAMMATION




(I')

(57) Abstract

A class of benzopyran derivatives is described for use in treating cyclooxygenase–2 mediated disorders. Compounds of particular interest are defined by Formula (I'), wherein X, $A^1$, $A^2$, $A^3$, $A^4$, R, R", $R^1$ and $R^2$ are as described in the specification.

aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, 5- or 6- membered heteroaryl, lower hydrooxyalkyl, optionally substituted phenyl and 5- or 6- membered nitrogen containing heterocyclosulfonyl;

wherein $R^5$ is selected from hydrido, lower alkyl, halo, lower haloalkyl, lower alkoxy, and phenyl; and

wherein $R^6$ is selected from hydrido, halo, cyano, hydrooxyiminomethyl, lower hydroxyalkyl, lower alkynyl, phenylalkynyl, lower alkyl, lower alkoxy, formyl and phenyl;

or an isomer or pharmaceutically acceptable salt thereof.

A class of compounds of particular interest consists of those compounds of Formula IIc wherein $R^3$ is selected from hydrido, and chloro; wherein $R^4$ is selected from chloro, methyl, tert-butyl, methylthio, trifluoromethyl, difluoromethyl, pentafluoromethyl, trifluoromethylsulfide, trifluoromethooxy, cyano, substituted or unsubstituted phenylcarbonyl, and substituted or unsubstituted phenyl; wherein $R^5$ is selected from hydrido, methyl, tert-butyl, chloro; and wherein $R^6$ is selected from hydrido, chloro, thienyl, hydroxyiminomethyl, substituted or unsubstituted phenylethynyl, and substituted or unsubstituted phenyl; or an isomer or pharmaceutically acceptable salt thereof.

A family of specific compounds of particular interest within Formula I consists of compounds and pharmaceutically-acceptable salts thereof as follows:

6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

7-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-ethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-isopropyloxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-bis(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dimethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-nitro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

ethyl 6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylate;

6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-difluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(N,N-diethylamino)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-aminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-(methylamino)sulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-N,N-diethylaminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-(2,2-dimethylpropylcarbonyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-7-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;

6-[[(2-furanylmethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-[(phenylmethyl)sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-[[(phenylethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-iodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-bromo-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-hydroxymethyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(methylthio)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(methylsulfinyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(pentafluoroethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5-methoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-benzoyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorobenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-hydroxybenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-phenoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-(4-chlorophenoxy)-2-trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy)-2H-1-benzopyran-3-carboxylic acid;

6-(4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(3-chloro-4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy]-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(hydroxyimino)methyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(hydroxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-(1H-benzimidazol-2-yl)-6-chloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

7-(1,1-dimethylethyl)-2-(pentafluoroethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(methoxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(benzyloxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethynyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(2-furanyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(5-chloro-1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(3,3-dimethyl-1-butynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-chlorophenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methoxyphenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methylthio)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methylsulfonyl)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-fluorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6,8-diiodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(5-chloro-2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-bromophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(ethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(4-methoxyphenyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-2-(trifluoromethyl)-4-ethenyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-2-(trifluoromethyl)-4-phenyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-4-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(2,2,2-trifluoro-1-hydroxyethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6,8-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6,7-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

8-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

7-chloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6,7-dichloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzothiopyran-3-carboxylic acid;

6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;

6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6,7-difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

1,2-dihydro-6-(trifluoromethoxy)-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-(trifluoromethyl)-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-cyano-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(trifluoromethyl)phenyl]methyl]-3-quinolinecarboxylic acid;

6-chloro-1-[(4-chlorophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(methoxy)phenyl]methyl]-3-quinolinecarboxylic acid;

6-chloro-1-[(4-cyanophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-1,2-dihydro-1-[(4-nitrophenyl)methyl]-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-1,2-dihydro-1-ethyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-2-(triflouromethyl)-1,2-dihydro[1,8]napthyridine-3-carboxylic acid;

2-trifluoromethyl-2H-naphtho[1,2-b]pyran-3-carboxylic acid;

2-trifluoromethyl-3H-naphtho[2,1-b]pyran-3-carboxylic acid;

2-trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid;

5-(hydroxymethyl)-8-methyl-2-(trifluoromethyl)-2H-pyrano[2,3-c]pyridine-3-carboxylic acid;

6-(trifluoromethyl)-6h-1,3-dioxolo[4,5-g][1]benzopyran-7-carboxylic acid; and

3-(trifluoromethyl)-3H-benzofuro[3,2-f][1]benzopyran-2-carboxylic acid.

A preferred family of specific compounds of particular interest within Formulas I and I' consists of compounds as follows:

(S)-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-7-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-ethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-isopropyloxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-bis(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-dimethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-nitro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-ethyl 6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylate;

(S)-6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-difluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-7-(N,N-diethylamino)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-aminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(methylamino)sulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-N,N-diethylaminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(2,2-dimethylpropylcarbonyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-dichloro-7-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6-[[(2-furanylmethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[(phenylmethyl)sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-[[(phenylethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-iodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-bromo-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid ;

(S)-6-hydroxymethyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(methylthio)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(methylsulfinyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-5,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(pentafluoroethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-5-methoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-benzoyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-chlorobenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-hydroxybenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-phenoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-6-(4-chlorophenoxy)-2-trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(3-chloro-4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-chlorophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy]- 2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-[(hydroxyimino)methyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(hydroxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-8-(1H-benzimidazol-2-yl)-6-chloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-7-(1,1-dimethylethyl)-2-(pentafluoroethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(methoxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(benzyloxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-ethenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-ethynyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(2-furanyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(5-chloro-1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(3,3-dimethyl-1-butynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-[(4-chlorophenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-[(4-methoxyphenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-[(4-methylthio)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-[(4-methylsulfonyl)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-bromo-8-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-fluorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-8-chloro-6-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-diiodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(5-chloro-2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(4-bromophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(ethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-8-(4-methoxyphenyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-2-(trifluoromethyl)-4-ethenyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-2-(trifluoromethyl)-4-phenyl-2H-1-benzopyran-3-carboxylic acid;

(S)-6-chloro-4-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-(2,2,2-trifluoro-1-hydroxyethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

(S)-6-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6,8-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6,7-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-8-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-7-chloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6,7-dichloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

(S)-2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid;

(S)-6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;

(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6,7-difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-1,2-dihydro-6-(trifluoromethoxy)-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-(trifluoromethyl)-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-cyano-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(trifluoromethyl)phenyl]methyl]-3-quinolinecarboxylic acid;

(S)-6-chloro-1-[(4-chlorophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(methoxy)phenyl]methyl]-3-quinolinecarboxylic acid;

(S)-6-chloro-1-[(4-cyanophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-1,2-dihydro-1-[(4-nitrophenyl)methyl]-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-1,2-dihydro-1-ethyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

(S)-6-chloro-2-(triflouromethyl)-1,2-dihydro[1,8]napthyridine-3-carboxylic acid;

(S)-2-trifluoromethyl-2H-naphtho[1,2-b]pyran-3-carboxylic acid;

(S)-2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid;

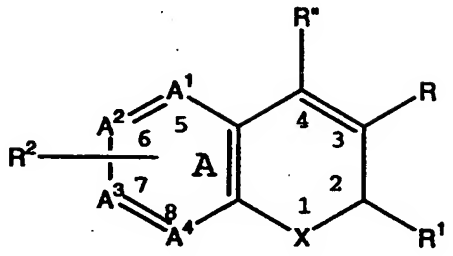
(S)-2-trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid; and

(S)-5-(hydroxymethyl)-8-methyl-2-(trifluoromethyl)-2H-pyrano[2,3-c]pyridine-3-carboxylic acid.

The term "hydrido" denotes a single hydrogen atom (H). This hydrido radical may be attached, for example, to an oxygen atom to form a hydroxyl radical or two hydrido radicals may be attached to a carbon atom to form a methylene ($-CH_2-$) radical. Where the term "alkyl" is used, either alone or within other terms such as "haloalkyl" and "alkylsulfonyl", it embraces linear or branched radicals having one to about twenty carbon atoms or, preferably, one to about twelve carbon atoms. More preferred alkyl radicals are "lower alkyl" radicals having one to about six carbon atoms. Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, *tert*-butyl, pentyl, iso-amyl, hexyl and the like. Most preferred are lower alkyl radicals having one to three carbon atoms. The term "alkenyl" embraces linear or branched radicals having at least one carbon-carbon double bond of two to about twenty carbon atoms or, preferably, two to about twelve carbon atoms. More preferred alkenyl radicals are "lower alkenyl" radicals having two to about six carbon atoms.

What is claimed is:

1. A compound of Formula I'



I'

wherein X is selected from O, S, $CR^cR^b$ and $NR^a$;
wherein $R^a$ is selected from hydrido, $C_1$-$C_3$-alkyl, (optionally substituted phenyl)-$C_1$-$C_3$-alkyl, acyl and carboxy-$C_1$-$C_6$-alkyl;
wherein each of $R^b$ and $R^c$ is independently selected from hydrido, $C_1$-$C_3$-alkyl, phenyl-$C_1$-$C_3$-alkyl, $C_1$-$C_3$-perfluoroalkyl, chloro, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkoxy, nitro, cyano and cyano-$C_1$-$C_3$-alkyl;
wherein R is selected from carboxyl, aminocarbonyl, $C_1$-$C_6$-alkylsulfonylaminocarbonyl and $C_1$-$C_6$-alkoxycarbonyl;
wherein R" is selected from hydrido, phenyl, thienyl and $C_2$-$C_6$-alkenyl;
wherein $R^1$ is selected from $C_1$-$C_3$-perfluoroalkyl, chloro, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkoxy, nitro, cyano and cyano-$C_1$-$C_3$-alkyl;
wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, $C_2$-$C_6$-alkenyl, $C_2$-$C_6$-alkynyl, halo-$C_2$-$C_6$-alkynyl, aryl-$C_1$-$C_3$-alkyl, aryl-$C_2$-$C_6$-alkynyl, aryl-$C_2$-$C_6$-alkenyl, $C_1$-$C_6$-alkoxy, methylenedioxy, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkylsulfinyl, aryloxy, arylthio, arylsulfinyl, heteroaryloxy, $C_1$-$C_6$-alkoxy-$C_1$-$C_6$-alkyl, aryl-$C_1$-$C_6$-alkyloxy, heteroaryl-$C_1$-$C_6$-alkyloxy, aryl-$C_1$-$C_6$-alkoxy-$C_1$-$C_6$-alkyl, $C_1$-$C_6$-haloalkyl, $C_1$-$C_6$-haloalkoxy, $C_1$-$C_6$-haloalkylthio, $C_1$-$C_6$-haloalkylsulfinyl, $C_1$-$C_6$-

haloalkylsulfonyl, $C_1$-$C_3$-(haloalkyl-$C_1$-$C_3$-hydroxyalkyl, $C_1$-$C_6$-hydroxyalkyl, hydroxyimino-$C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkylamino, arylamino, aryl-$C_1$-$C_6$-alkylamino, heteroarylamino, heteroaryl-$C_1$-$C_6$-alkylamino, nitro, cyano, amino, aminosulfonyl, $C_1$-$C_6$-alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aryl-$C_1$-$C_6$-alkylaminosulfonyl, heteroaryl-$C_1$-$C_6$-alkylaminosulfonyl, heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, aryl-$C_1$-$C_6$-alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aryl-$C_1$-$C_6$-alkylcarbonyl, heteroaryl-$C_1$-$C_6$-alkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, $C_1$-$C_6$-alkoxycarbonyl, formyl, $C_1$-$C_6$-haloalkylcarbonyl and $C_1$-$C_6$-alkylcarbonyl; and

wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least two of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon;

or wherein $R^2$ together with ring A forms a radical selected from naphthyl, quinolyl, isoquinolyl, quinolizinyl, quinoxalinyl and dibenzofuryl;

or an isomer or pharmaceutically acceptable salt thereof.

2. A compound of Claim 1 wherein X is selected from O, S, $CR^cR^b$ and $NR^a$; wherein $R^a$ is selected from hydrido, $C_1$-$C_3$-alkyl, (optionally substituted phenyl)-$C_1$-$C_3$-alkyl, acyl and carboxy-$C_1$-$C_6$-alkyl; wherein each of $R^b$ and $R^b$ is independently selected from hydrido, $C_1$-$C_3$-alkyl, phenyl-$C_1$-$C_3$-alkyl, $C_1$-$C_3$-perfluoroalkyl, chloro, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkoxy, nitro, cyano and cyano-$C_1$-$C_3$-alkyl; wherein R is selected from carboxyl, aminocarbonyl, $C_1$-$C_6$-alkylsulfonylaminocarbonyl and $C_1$-$C_6$-alkoxycarbonyl; wherein $R^a$ is selected from hydrido, phenyl, thienyl and $C_2$-$C_6$-alkenyl; wherein $R^1$ is selected from $C_1$-$C_3$-

perfluoroalkyl, chloro, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkoxy, nitro, cyano and cyano-$C_1$-$C_3$-alkyl; wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, $C_2$-$C_6$-alkenyl, $C_2$-$C_6$-alkynyl, halo-$C_2$-$C_6$-alkynyl, aryl-$C_1$-$C_3$-alkyl, aryl-$C_2$-$C_6$-alkynyl, aryl-$C_2$-$C_6$-alkenyl, $C_1$-$C_6$-alkoxy, methylenedioxy, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkylsulfinyl, aryloxy, arylthio, arylsulfinyl, heteroaryloxy, $C_1$-$C_6$-alkoxy-$C_1$-$C_6$-alkyl, aryl-$C_1$-$C_6$-alkyloxy, heteroaryl-$C_1$-$C_6$-alkyloxy, aryl-$C_1$-$C_6$-alkoxy-$C_1$-$C_6$-alkyl, $C_1$-$C_6$-haloalkyl, $C_1$-$C_6$-haloalkoxy, $C_1$-$C_6$-haloalkylthio, $C_1$-$C_6$-haloalkylsulfinyl, $C_1$-$C_6$-haloalkylsulfonyl, $C_1$-$C_3$-(haloalkyl-$C_1$-$C_3$-hydroxyalkyl, $C_1$-$C_6$-hydroxyalkyl, hydroxyimino-$C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkylamino, arylamino, aryl-$C_1$-$C_6$-alkylamino, heteroarylamino, heteroaryl-$C_1$-$C_6$-alkylamino, nitro, cyano, amino, aminosulfonyl, $C_1$-$C_6$-alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aryl-$C_1$-$C_6$-alkylaminosulfonyl, heteroaryl-$C_1$-$C_6$-alkylaminosulfonyl, heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, aryl-$C_1$-$C_6$-alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aryl-$C_1$-$C_6$-alkylcarbonyl, heteroaryl-$C_1$-$C_6$-alkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, $C_1$-$C_6$-alkoxycarbonyl, formyl, $C_1$-$C_6$-haloalkylcarbonyl and $C_1$-$C_6$-alkylcarbonyl; and wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or wherein $R^2$ together with ring A forms a naphthyl or quinolyl radical; or an isomer or pharmaceutically acceptable salt thereof.

3. A compound of Claim 2 wherein X is selected from O, S and $NR^a$; wherein $R^a$ is selected from hydrido, $C_1$-$C_3$-alkyl and (optionally substituted phenyl)methyl; wherein R is carboxyl; wherein $R''$ is selected from hydrido and $C_2$-$C_6$-alkenyl; wherein $R^1$ is

selected from $C_1$-$C_3$-perfluoroalkyl; wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, $C_2$-$C_6$-alkenyl, $C_2$-$C_6$-alkynyl, halo-$C_2$-$C_6$-alkynyl, phenyl-$C_1$-$C_6$-alkyl, phenyl-$C_2$-$C_6$-alkynyl, phenyl-$C_2$-$C_6$-alkenyl, $C_1$-$C_3$-alkoxy, methylenedioxy, $C_1$-$C_3$-alkoxy-$C_1$-$C_3$-alkyl, $C_1$-$C_3$-alkylthio, $C_1$-$C_3$-alkylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, $C_1$-$C_3$-haloalkyl-$C_1$-$C_3$-hydroxyalkyl, phenyl-$C_1$-$C_3$-alkyloxy-$C_1$-$C_3$-alkyl, $C_1$-$C_3$-haloalkyl, $C_1$-$C_3$-haloalkoxy, $C_1$-$C_3$-haloalkylthio, $C_1$-$C_3$-hydroxyalkyl, $C_1$-$C_3$-alkoxy-$C_1$-$C_3$-alkyl, hydroxyimino-$C_1$-$C_3$-alkyl, $C_1$-$C_6$-alkylamino, nitro, cyano, amino, aminosulfonyl, N-alkylaminosulfonyl, N-arylaminosulfonyl, N-heteroarylaminosulfonyl, N-(phenyl-$C_1$-$C_6$-alkyl)aminosulfonyl, N-(heteroaryl-$C_1$-$C_6$-alkyl)aminosulfonyl, phenyl-$C_1$-$C_3$-alkylsulfonyl, 5- to 8-membered heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, optionally substituted phenyl, optionally substituted 5- to 9-membered heteroaryl, phenyl-$C_1$-$C_6$-alkylcarbonyl, phenylcarbonyl, 4-chlorophenylcarbonyl, 4-hydroxyphenylcarbonyl, 4-trifluoromethylphenylcarbonyl, 4-methoxyphenylcarbonyl, aminocarbonyl, formyl, and $C_1$-$C_6$-alkylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or wherein $R^2$ together with ring A forms a naphthyl, benzofurylphenyl, or quinolyl radical; or an isomer or pharmaceutically acceptable salt thereof.

4. A compound of Claim 3 wherein X is selected from O, S and $NR^a$; wherein $R^a$ is selected from hydrido, methyl, ethyl, (4-trifluoromethyl)benzyl, (4-chloromethyl)benzyl, (4-methoxy)benzyl, and (4-cyano)benzyl, (4-nitro)benzyl; wherein R is carboxyl; wherein $R''$ is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl

and pentafluoroethyl; wherein $R^2$ is one or more radicals independently selected from hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, ethenyl, ethynyl, 5-chloro-1-pentynyl, 1-pentynyl, 3,3-dimethyl-1-butynyl, benzyl, phenylethyl, phenyl-ethynyl, 4-chlorophenyl-ethynyl, 4-methoxyphenyl-ethynyl, phenylethenyl, methoxy, methylthio, methylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, methylenedioxy, benzyloxymethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, trifluoromethoxy, trifluoromethylthio, hydroxymethyl, hydroxy-trifluoroethyl, methoxymethyl, hydroxyiminomethyl, N-methylamino, nitro, cyano, amino, aminosulfonyl, N-methylaminosulfonyl, N-phenylaminosulfonyl, N-furylaminosulfonyl, N-(benzyl)aminosulfonyl, N-(furylmethyl)aminosulfonyl, benzylsulfonyl, phenylethylaminosulfonyl, furylsulfonyl, methylsulfonyl, phenyl, phenyl substituted with one or more radicals selected from chloro, fluoro, bromo, methoxy, methylthio and methylsulfonyl, benzimidazolyl, thienyl, thienyl substituted with chloro, furyl, furyl substituted with chloro, benzylcarbonyl, optionally substituted phenylcarbonyl, aminocarbonyl, formyl and methylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or wherein $R^2$ together with ring A forms a naphthyl, or quinolyl radical; or an isomer or pharmaceutically acceptable salt thereof.

5. A compound of Claim 4 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of 6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
7-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
8-ethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
7,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
7-isopropyloxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-bis(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dimethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-nitro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

ethyl 6-amino-2-trifluoromethyl-2H-1-benzopyran-3-carboxylate;

6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-difluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(N,N-diethylamino)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-aminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-(methylamino)sulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-N,N-diethylaminosulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-(2,2-dimethylpropylcarbonyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6,8-dichloro-7-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;
6-[[(2-furanylmethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-[(phenylmethyl)sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-[[(phenylethyl)amino]sulfonyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-iodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
8-bromo-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-formyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-bromo-7-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
5,6-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid ;
6-hydroxymethyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(methylthio)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(methylsulfinyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,8-dichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(pentafluoroethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-2,7-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5-methoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-benzoyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorobenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-hydroxybenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-phenoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-(4-chlorophenoxy)-2-trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy)-2H-1-benzopyran-3-carboxylic acid;

6-(4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(3-chloro-4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy]- 2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(hydroxyimino)methyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(hydroxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-(1H-benzimidazol-2-yl)-6-chloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

7-(1,1-dimethylethyl)-2-(pentafluoroethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(methoxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(benzyloxymethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethynyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(2-furanyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(5-chloro-1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(1-pentynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(3,3-dimethyl-1-butynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-chlorophenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methoxyphenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methylthio)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-[(4-methylsulfonyl)phenyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-fluorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-fluoro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6,8-diiodo-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(5-chloro-2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(4-bromophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(ethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(4-methoxyphenyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-2-(trifluoromethyl)-4-ethenyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-2-(trifluoromethyl)-4-phenyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-4-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(2,2,2-trifluoro-1-hydroxyethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6,8-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6,7-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
8-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
7-chloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6,7-dichloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid;
6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;
6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6,7-difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
1,2-dihydro-6-(trifluoromethoxy)-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-(trifluoromethyl)-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-cyano-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(trifluoromethyl)phenyl]methyl]-3-quinolinecarboxylic acid;
6-chloro-1-[(4-chlorophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(methoxy)phenyl]methyl]-3-quinolinecarboxylic acid;
6-chloro-1-[(4-cyanophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-[(4-nitrophenyl)methyl]-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-ethyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6-chloro-2-(triflouromethyl)-1,2-dihydro[1,8]napthyridine-3-carboxylic acid;
2-trifluoromethyl-2H-naphtho[1,2-b]pyran-3-carboxylic acid;
2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid;
2-trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid;
5-(hydroxymethyl)-8-methyl-2-(trifluoromethyl)-2H-pyrano[2,3-c]pyridine-3-carboxylic acid;
6-(trifluoromethyl)-6h-1,3-dioxolo[4,5-g][1]benzopyran-7-carboxylic acid; and
3-(trifluoromethyl)-3H-benzofuro[3,2-f][1]benzopyran-2-carboxylic acid.

6. A compound of Claim 2 wherein X is O; wherein R is carboxyl; wherein R'' is selected from hydrido and $C_2$-$C_6$-alkenyl; wherein $R^1$ is selected from $C_1$-$C_3$-perfluoroalkyl; wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, phenyl-$C_1$-$C_6$-alkyl, phenyl-$C_2$-$C_6$-alkynyl, phenyl-$C_2$-$C_6$-alkenyl, $C_1$-$C_6$-alkoxy, phenyloxy, 5- or 6-membered heteroaryloxy, phenyl-$C_1$-$C_6$-alkyloxy, 5- or 6-membered heteroaryl-$C_1$-$C_6$-alkyloxy, $C_1$-$C_6$-haloalkyl, $C_1$-$C_6$-haloalkoxy, N-($C_1$-$C_6$-alkyl)amino, N,N-di-($C_1$-$C_6$-alkyl)amino, N-phenylamino, N-(phenyl-$C_1$-$C_6$-alkyl)amino, N-heteroarylamino, N-(heteroaryl-$C_1$-$C_6$-alkylamino, nitro, amino, aminosulfonyl, N-($C_1$-$C_6$-alkyl)aminosulfonyl, N,N-di-($C_1$-$C_6$-alkyl)aminosulfonyl, N-arylaminosulfonyl, N-heteroarylaminosulfonyl, N-(phenyl-$C_1$-$C_6$-alkyl)aminosulfonyl, N-(heteroaryl-$C_1$-$C_6$-alkyl)aminosulfonyl, 5- to 8-membered heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, phenyl-$C_1$-$C_6$-alkylcarbonyl, heteroarylcarbonyl, phenylcarbonyl, aminocarbonyl,

and $C_1$-$C_6$-alkylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

7. A compound of Claim 6 wherein X is O; wherein R is carboxyl; wherein R" is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl and pentafluoroethyl; wherein $R^2$ is one or more radicals independently selected from hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, ethenyl, ethynyl, 5-chloro-1-pentynyl, 1-pentynyl, 3,3-dimethyl-1-butynyl, benzyl, phenylethyl, phenyl-ethynyl, 4-chlorophenyl-ethynyl, 4-methoxyphenyl-ethynyl, phenylethenyl, methoxy, methylthio, methylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, pyridyloxy, thienyloxy, furyloxy, phenylmethoxy, methylenedioxy, benzyloxymethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, trifluoromethoxy, trifluoromethylthio, hydroxymethyl, hydroxy-trifluoroethyl, methoxymethyl, hydroxyiminomethyl, N-methylamino, N-phenylamino, N-(benzyl)amino, nitro, cyano, amino, aminosulfonyl, N-methylaminosulfonyl, N-phenylaminosulfonyl, N-furylaminosulfonyl, N-(benzyl)aminosulfonyl, N-(furylmethyl)aminosulfonyl, benzylsulfonyl, phenylethylaminosulfonyl, furylsulfonyl, methylsulfonyl, phenyl, phenyl substituted with one or more radicals selected from chloro, fluoro, bromo, methoxy, methylthio and methylsulfonyl, benzimidazolyl, thienyl, thienyl substituted with chloro, furyl, furyl substituted with chloro, benzylcarbonyl, furylcarbonyl, phenylcarbonyl, aminocarbonyl, formyl, and methylcarbonyl; and wherein one of the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ is nitrogen and the other three are

carbon; or an isomer or pharmaceutically acceptable salt thereof.

9. A compound of Claim 7 wherein X is O; wherein R is carboxyl; wherein R" is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl and pentafluoroethyl; wherein $R^2$ is one or more radicals independently selected from hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, ethenyl, ethynyl, 5-chloro-1-pentynyl, 1-pentynyl, 3,3-dimethyl-1-butynyl, benzyl, phenylethyl, phenyl-ethynyl, 4-chlorophenyl-ethynyl, 4-methoxyphenyl-ethynyl, phenylethenyl, methoxy, methylthio, methylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, pyridyloxy, thienyloxy, furyloxy, phenylmethoxy, methylenedioxy, benzyloxymethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, trifluoromethoxy, trifluoromethylthio, hydroxymethyl, hydroxy-trifluoroethyl, methoxymethyl, hydroxyiminomethyl, N-methylamino, N-phenylamino, N-(benzyl)amino, nitro, cyano, amino, aminosulfonyl, N-methylaminosulfonyl, N-phenylaminosulfonyl, N-furylaminosulfonyl, N-(benzyl)aminosulfonyl, N-(furylmethyl)aminosulfonyl, benzylsulfonyl, phenylethylaminosulfonyl, furylsulfonyl, methylsulfonyl, phenyl, phenyl substituted with one or more radicals selected from chloro, fluoro, bromo, methoxy, methylthio and methylsulfonyl, benzimidazolyl, thienyl, thienyl substituted with chloro, furyl, furyl substituted with chloro, benzylcarbonyl, furylcarbonyl, phenylcarbonyl, aminocarbonyl, formyl, and methylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

10. A compound of Claim 9 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of
6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
(S)-6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
(S)-6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
(S)-6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
(S)-6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6,8-dichloro-7-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;
6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;
(S)-6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;
6-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
(S)-6-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-hydroxymethyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(difluoromethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2,6-bis(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

5,6,7-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6,7,8-trichloro-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(methylthio)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(pentafluoroethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-7-methyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-benzoyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorobenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-hydroxybenzoyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-phenoxy-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy)-2H-1-benzopyran-3-carboxylic acid;

(S)-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy)-2H-1-benzopyran-3-carboxylic acid;

6-(4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(3-chloro-4-methoxyphenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

6-(4-chlorophenoxy)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;

8-chloro-2-(trifluoromethyl)-6-[4-(trifluoromethyl)phenoxy]-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-cyano-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(2-thienyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-[(4-chlorophenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-[(4-methoxyphenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
(S)-6-chloro-8-[(4-methoxyphenyl)ethynyl]-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(phenylethynyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-phenyl-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-(4-bromophenyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid;
6-chloro-8-(4-methoxyphenyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid; and
6-(2,2,2-trifluoro-1-hydroxyethyl)-2-(trifluoromethyl)-2H-1-benzopyran-3-carboxylic acid.

11. A compound of Claim 2 wherein X is S; wherein R is carboxyl; wherein $R^1$ is selected from $C_1$-$C_3$-perfluoroalkyl; wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, phenyl-$C_1$-$C_6$-alkyl, phenyl-$C_2$-$C_6$-alkynyl, phenyl-$C_2$-$C_6$-alkenyl, $C_1$-$C_6$-alkoxy, phenyloxy, 5- or

6-membered heteroaryloxy, phenyl-$C_1$-$C_6$-alkyloxy, 5- or 6-membered heteroaryl-$C_1$-$C_6$-alkyloxy, $C_1$-$C_6$-haloalkyl, $C_1$-$C_6$-haloalkoxy, $C_1$-$C_6$-alkylamino, N-phenylamino, N-(phenyl-$C_1$-$C_6$-alkyl)amino, N-heteroarylamino, N-(heteroaryl-$C_1$-$C_6$-alkylamino, nitro, amino, aminosulfonyl, N-alkylaminosulfonyl, N-arylaminosulfonyl, N-heteroarylaminosulfonyl, N-(phenyl-$C_1$-$C_6$-alkyl)aminosulfonyl, N-(heteroaryl-$C_1$-$C_6$-alkyl)aminosulfonyl, 5- to 8-membered heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, phenyl-$C_1$-$C_6$-alkylcarbonyl, heteroarylcarbonyl, phenylcarbonyl, aminocarbonyl, and $C_1$-$C_6$-alkylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

12. A compound of Claim 11 wherein X is S; wherein R is carboxyl; wherein R" is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl and pentafluoroethyl; wherein $R^2$ is one or more radicals independently selected from hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, ethenyl, ethynyl, 5-chloro-1-pentynyl, 1-pentynyl, 3,3-dimethyl-1-butynyl, benzyl, phenylethyl, phenyl-ethynyl, 4-chlorophenyl-ethynyl, 4-methoxyphenyl-ethynyl, phenylethenyl, methoxy, methylthio, methylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, pyridyloxy, thienyloxy, furyloxy, phenylmethoxy, methylenedioxy, benzyloxymethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, trifluoromethoxy, trifluoromethylthio, hydroxymethyl, hydroxy-trifluoroethyl, methoxymethyl, hydroxyiminomethyl, N-methylamino, N-phenylamino, N-(benzyl)amino, nitro, cyano, amino, aminosulfonyl, N-methylaminosulfonyl, N-

phenylaminosulfonyl, N-furylaminosulfonyl, N-(benzyl)aminosulfonyl, N-(furylmethyl)aminosulfonyl, benzylsulfonyl, phenylethylaminosulfonyl, furylsulfonyl, methylsulfonyl, phenyl, phenyl substituted with one or more radicals selected from chloro, fluoro, bromo, methoxy, methylthio and methylsulfonyl, benzimidazolyl, thienyl, thienyl substituted with chloro, furyl, furyl substituted with chloro, benzylcarbonyl, furylcarbonyl, phenylcarbonyl, aminocarbonyl, formyl, and methylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

13. A compound of Claim 12 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of

6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid;
6-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6,8-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6-(1,1-dimethylethyl)-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6,7-dimethyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
8-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
6-chloro-7-methyl-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
7-chloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;

6,7-dichloro-2-(trifluoromethyl)-2H-1-benzothiopyran-3-carboxylic acid;
2-(trifluoromethyl)-6-[(trifluoromethyl)thio]-2H-1-benzopyran-3-carboxylic acid; and
6,8-dichloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

14. A compound of Claim 2 wherein X is $NR^*$; wherein $R^*$ is selected from hydrido, $C_1$-$C_3$-alkyl, phenyl-$C_1$-$C_3$-alkyl, acyl and carboxy-$C_1$-$C_3$-alkyl; wherein R is carboxyl; wherein $R^1$ is selected from $C_1$-$C_3$-perfluoroalkyl; wherein $R^2$ is one or more radicals independently selected from hydrido, halo, $C_1$-$C_6$-alkyl, phenyl-$C_1$-$C_6$-alkyl, phenyl-$C_2$-$C_6$-alkynyl, phenyl-$C_2$-$C_6$-alkenyl, $C_1$-$C_6$-alkoxy, phenyloxy, 5- or 6-membered heteroaryloxy, phenyl-$C_1$-$C_6$-alkyloxy, 5- or 6-membered heteroaryl-$C_1$-$C_6$-alkyloxy, $C_1$-$C_6$-haloalkyl, $C_1$-$C_6$-haloalkoxy, $C_1$-$C_6$-alkylamino, N-phenylamino, N-(phenyl-$C_1$-$C_6$-alkyl)amino, N-heteroarylamino, N-(heteroaryl-$C_1$-$C_6$-alkylamino, nitro, amino, aminosulfonyl, N-alkylaminosulfonyl, N-arylaminosulfonyl, N-heteroarylaminosulfonyl, N-(phenyl-$C_1$-$C_6$-alkyl)aminosulfonyl, N-(heteroaryl-$C_1$-$C_6$-alkyl)aminosulfonyl, 5- to 8-membered heterocyclylsulfonyl, $C_1$-$C_6$-alkylsulfonyl, optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, phenyl-$C_1$-$C_6$-alkylcarbonyl, heteroarylcarbonyl, phenylcarbonyl, aminocarbonyl, and $C_1$-$C_6$-alkylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

15. A compound of Claim 14 wherein X is $NR^*$; wherein $R^*$ is selected from hydrido, methyl, ethyl, (4-trifluoromethyl)benzyl, (4-chloromethyl)benzyl, (4-methoxy)benzyl, (4-cyano)benzyl, and (4-

nitro)benzyl; wherein R is carboxyl; wherein R" is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl and pentafluoroethyl; wherein $R^2$ is one or more radicals independently selected from hydrido, chloro, bromo, fluoro, iodo, methyl, tert-butyl, ethenyl, ethynyl, 5-chloro-1-pentynyl, 1-pentynyl, 3,3-dimethyl-1-butynyl, benzyl, phenylethyl, phenyl-ethynyl, 4-chlorophenyl-ethynyl, 4-methoxyphenyl-ethynyl, phenylethenyl, methoxy, methylthio, methylsulfinyl, phenyloxy, phenylthio, phenylsulfinyl, pyridyloxy, thienyloxy, furyloxy, phenylmethoxy, methylenedioxy, benzyloxymethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, trifluoromethoxy, trifluoromethylthio, hydroxymethyl, hydroxy-trifluoroethyl, methoxymethyl, hydroxyiminomethyl, N-methylamino, N-phenylamino, N-(benzyl)amino, nitro, cyano, amino, aminosulfonyl, N-methylaminosulfonyl, N-phenylaminosulfonyl, N-furylaminosulfonyl, N-(benzyl)aminosulfonyl, N-(furylmethyl)aminosulfonyl, benzylsulfonyl, phenylethylaminosulfonyl, furylsulfonyl, methylsulfonyl, phenyl, phenyl substituted with one or more radicals selected from chloro, fluoro, bromo, methoxy, methylthio and methylsulfonyl, benzimidazolyl, thienyl, thienyl substituted with chloro, furyl, furyl substituted with chloro, benzylcarbonyl, furylcarbonyl, phenylcarbonyl, aminocarbonyl, formyl, and methylcarbonyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or an isomer or pharmaceutically acceptable salt thereof.

16. A compound of Claim 15 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of

6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;

6,8-dichloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6,7-difluoro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-iodo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-bromo-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
1,2-dihydro-6-(trifluoromethoxy)-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-(trifluoromethyl)-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-cyano-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-methyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(trifluoromethyl)phenyl]methyl]-3-quinolinecarboxylic acid;
6-chloro-1-[(4-chlorophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-2-(trifluoromethyl)-1-[[4-(methoxy)phenyl]methyl]-3-quinolinecarboxylic acid;
6-chloro-1-[(4-cyanophenyl)methyl]-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-[(4-nitrophenyl)methyl]-2-(trifluoromethyl)-3-quinolinecarboxylic acid;
6-chloro-1,2-dihydro-1-ethyl-2-(trifluoromethyl)-3-quinolinecarboxylic acid; and
(S)-6-chloro-1,2-dihydro-2-(trifluoromethyl)-3-quinolinecarboxylic acid.

17. A compound of Claim 2 wherein X is selected from O, S and $NR^a$; wherein $R^a$ is selected from hydrido, $C_1$-$C_3$-alkyl, phenyl-$C_1$-$C_3$-alkyl, acyl and carboxy-$C_1$-$C_3$-alkyl; wherein R is selected from carboxyl; wherein $R^1$ is selected from $C_1$-$C_3$-

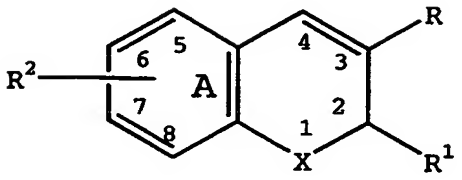
perfluoroalkyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; and wherein $R^2$ together with ring A forms a naphthyl or quinolyl radical; or an isomer or pharmaceutically acceptable salt thereof.

18. A compound of Claim 17 wherein X is selected from O, S and $NR^*$; wherein $R^*$ is selected from hydrido, methyl, ethyl, (4-trifluoromethyl)benzyl, (4-chloromethyl)benzyl, (4-methoxy)benzyl, and (4-cyano)benzyl, (4-nitro)benzyl; wherein R is carboxyl; wherein $R''$ is selected from hydrido and ethenyl; wherein $R^1$ is selected from trifluoromethyl and pentafluoroethyl; wherein the A ring atoms $A^1$, $A^2$, $A^3$ and $A^4$ are independently selected from carbon and nitrogen with the proviso that at least three of $A^1$, $A^2$, $A^3$ and $A^4$ are carbon; or wherein $R^2$ together with ring A forms a naphthyl, or quinolyl radical; or an isomer or pharmaceutically acceptable salt thereof.

19. A compound of Claim 18 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of

2-trifluoromethyl-2H-naphtho[1,2-b]pyran-3-carboxylic acid;
2-trifluoromethyl-3H-naphtho[2,1-b]pyran-3-carboxylic acid;
2-trifluoromethyl-2H-naphtho[2,3-b]pyran-3-carboxylic acid;
5-(hydroxymethyl)-8-methyl-2-(trifluoromethyl)-2H-pyrano[2,3-c]pyridine-3-carboxylic acid;
6-(trifluoromethyl)-6h-1,3-dioxolo[4,5-g][1]benzopyran-7-carboxylic acid; and
3-(trifluoromethyl)-3H-benzofuro[3,2-f][1]benzopyran-2-carboxylic acid.

20. A compound of Formula I



I

wherein X is selected from O or S or NR*;

wherein R* is alkyl;

wherein R is selected from carboxyl, aminocarbonyl, alkylsulfonylaminocarbonyl and alkoxycarbonyl;

wherein $R^1$ is selected from haloalkyl, alkyl, aralkyl, cycloalkyl and aryl optionally substituted with one or more radicals selected from alkylthio, nitro and alkylsulfonyl; and

wherein $R^2$ is one or more radicals selected from hydrido, halo, alkyl, aralkyl, alkoxy, aryloxy, heteroaryloxy, aralkyloxy, heteroaralkyloxy, haloalkyl, haloalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroarylalkylamino, nitro, amino, aminosulfonyl, alkylaminosulfonyl, arylaminosulfonyl, heteroarylaminosulfonyl, aralkylaminosulfonyl, heteroaralkylaminosulfonyl, heterocyclosulfonyl, alkylsulfonyl, optionally substituted aryl, optionally substituted heteroaryl, aralkylcarbonyl, heteroarylcarbonyl, arylcarbonyl, aminocarbonyl, and alkylcarbonyl;

or wherein $R^2$ together with ring A forms a naphthyl radical;

or an isomer or pharmaceutically acceptable salt thereof.

21. Compound of Claim 20 wherein X is oxygen or sulfur; wherein R is selected from carboxyl, lower alkyl, lower aralkyl and lower alkoxycarbonyl;

wherein $R^1$ is selected from lower haloalkyl, lower cycloalkyl and phenyl; and wherein $R^2$ is one or more radicals selected from hydrido, halo, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkylamino, nitro, amino, aminosulfonyl, lower alkylaminosulfonyl, 5- or 6- membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, 5- or 6- membered nitrogen containing heterocyclosulfonyl, lower alkylsulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, and lower alkylcarbonyl; or wherein $R^2$ together with ring A forms a naphthyl radical; or an isomer or pharmaceutically acceptable salt thereof.

22. Compound of Claim 21 wherein X is oxygen or sulfur; wherein R is carboxyl; wherein $R^1$ is lower haloalkyl; and wherein $R^2$ is one or more radicals selected from hydrido, halo, lower alkyl, lower haloalkyl, lower haloalkoxy, lower alkylamino, amino, aminosulfonyl, lower alkylaminosulfonyl, 5- or 6-membered heteroarylalkylaminosulfonyl, lower aralkylaminosulfonyl, lower alkylsulfonyl, 6-membered nitrogen containing heterocyclosulfonyl, optionally substituted phenyl, lower aralkylcarbonyl, and lower alkylcarbonyl; or wherein $R^2$ together with ring A forms a naphthyl radical; or an isomer or pharmaceutically acceptable salt thereof.

23. Compound of Claim 22 wherein R is carboxyl; wherein $R^1$ is selected from fluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, difluoromethyl, and trifluoromethyl; and wherein $R^2$ is one or more radicals selected from hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, butyl, isobutyl, pentyl, hexyl, methoxy, ethoxy, isopropyloxy, tertbutyloxy, trifluoromethyl,

difluoromethyl, trifluoromethoxy, amino, N,N-dimethylamino, N,N-diethylamino, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, nitro, N,N-dimethylaminosulfonyl, aminosulfonyl, N-methylaminosulfonyl, N-ethylsulfonyl, 2,2-dimethylethylaminosulfonyl, N,N-dimethylaminosulfonyl, N-(2-methylpropyl)aminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, 2,2-dimethylpropylcarbonyl, phenylacetyl and phenyl; or wherein $R^2$ together with ring A forms a naphthyl radical; or an isomer or pharmaceutically acceptable salt thereof.

24. Compound of Claim 23 wherein R is carboxyl; wherein $R^1$ is trifluoromethyl or pentafluorethyl; and wherein $R^2$ is one or more radicals selected from hydrido, chloro, fluoro, bromo, iodo, methyl, ethyl, isopropyl, *tert*-butyl, methoxy, trifluoromethyl, trifluoromethoxy, N-phenylmethylaminosulfonyl, N-phenylethylaminosulfonyl, N-(2-furylmethyl)aminosulfonyl, N,N-dimethylaminosulfonyl, N-methylaminosulfonyl, N-(2,2-dimethylethyl)aminosulfonyl, dimethylaminosulfonyl, 2-methylpropylaminosulfonyl, N-morpholinosulfonyl, methylsulfonyl, benzylcarbonyl, and phenyl; or wherein $R^2$ together with ring A forms a naphthyl radical; or an isomer or pharmaceutically acceptable salt thereof.

25. A compound of Claim 24 selected from compounds, and their isomers and pharmaceutically-acceptable salts, of the group consisting of 6-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

2-trifluoromethyl-3H-naphthopyran-3-carboxylic acid ;

7-(1,1-dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-trifluoromethoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

5,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7,8-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-bis(dimethylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(1-methylethyl)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-ethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-7-phenyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,7-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

2-trifluoromethyl-3H-naptho[2,1-b]pyran-3-carboxylic acid;

6-chloro-8-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-chloro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-6-methyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-bromo-5-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-chloro-8-fluoro-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-bromo-8-methoxy-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(dimethylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(methylamino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(4-morpholino)sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(1,1-dimethylethyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[(2-methylpropyl)aminosulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-methylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-6-[[(phenylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-phenylacetyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dibromo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

8-chloro-5,6-dimethyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6,8-dichloro-(*S*)-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-benzylsulfonyl-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-[[N-(2-furylmethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

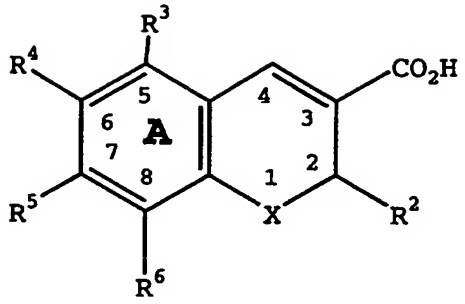
6-[[N-(2-phenylethyl)amino]sulfonyl]-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

6-iodo-2-trifluoromethyl-2H-1-benzopyran-3-carboxylic acid;

7-(1,1-dimethylethyl)-2-pentafluoroethyl-2H-1-benzopyran-3-carboxylic acid; and

6-chloro-2-trifluoromethyl-2H-1-benzothiopyran-3-carboxylic acid.

26. A compound of Formula II



II

wherein X is O or S;

wherein $R^2$ is lower haloalkyl;

wherein $R^3$ is selected from hydrido, and halo;

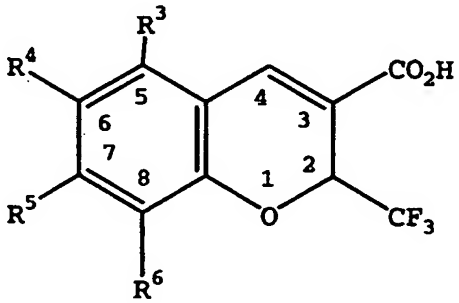
wherein $R^4$ is selected from hydrido, halo, lower alkyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, and 5- or 6- membered nitrogen-containing heterocyclosulfonyl;

wherein $R^5$ is selected from hydrido, lower alkyl, halo, lower alkoxy, and aryl; and

wherein $R^6$ is selected from hydrido, halo, lower alkyl, lower alkoxy, and aryl;

or an isomer or pharmaceutically acceptable salt thereof.

27. A compound of Formula IIa:



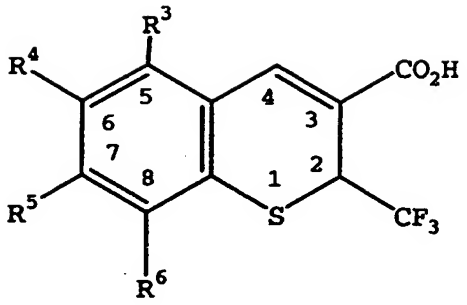
IIa

wherein $R^3$ is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkoxy and halo;

wherein $R^4$ is selected from hydrido, halo, lower alkyl, lower alkylthio, lower haloalkyl, amino, aminosulfonyl, lower alkylsulfonyl, lower alkylsulfinyl, lower alkoxyalkyl, lower alkylcarbonyl, formyl, cyano, lower haloalkylthio, substituted or unsubstituted phenylcarbonyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, 5- or 6- membered heteroaryl, lower hydrooxyalkyl, optionally substituted phenyl and 5- or 6- membered nitrogen containing heterocyclosulfonyl; wherein $R^5$ is selected from hydrido, lower alkyl, halo, lower haloalkyl, lower alkoxy, and phenyl; and wherein $R^6$ is selected from hydrido, halo, cyano, hydrooxyiminomethyl, lower hydroxyalkyl, lower alkynyl, phenylalkynyl, lower alkyl, lower alkoxy, formyl and phenyl; or an isomer or pharmaceutically acceptable salt thereof.

28. Compound of Claim 27 wherein $R^3$ is selected from hydrido, and chloro; wherein $R^4$ is selected from chloro, methyl, tert-butyl, methylthio, trifluoromethyl, difluoromethyl, pentafluoromethyl, trifluoromethylsulfide, trifluoromethooxy, cyano, substituted or unsubstituted phenylcarbonyl, and substituted or unsubstituted phenyl; wherein $R^5$ is selected from hydrido, methyl, tert-butyl, chloro; and wherein $R^6$ is selected from hydrido, chloro, thienyl, hydroxyiminomethyl, substituted or unsubstituted phenylethynyl, and substituted or unsubstituted phenyl; or an isomer or pharmaceutically acceptable salt thereof.

29. A compound of Formula IIb:



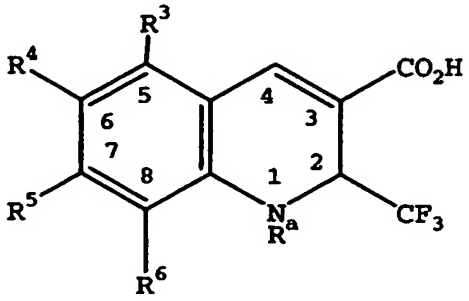
IIb

wherein $R^3$ is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkoxy and halo; wherein $R^4$ is selected from hydrido, halo, lower alkyl, lower alkylthio, lower haloalkyl, amino, aminosulfonyl, lower alkylsulfonyl, lower alkylsulfinyl, lower alkoxyalkyl, lower alkylcarbonyl, formyl, cyano, lower haloalkylthio, substituted or unsubstituted phenylcarbonyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, 5- or 6- membered heteroaryl, lower hydrooxyalkyl, optionally substituted phenyl and 5- or 6- membered nitrogen containing heterocyclosulfonyl; wherein $R^5$ is selected from hydrido, lower alkyl, halo, lower haloalkyl, lower alkoxy, and phenyl; and wherein $R^6$ is selected from hydrido, halo, cyano, hydrooxyiminomethyl, lower hydroxyalkyl, lower alkynyl, phenylalkynyl, lower alkyl, lower alkoxy, formyl and phenyl;_or an isomer or pharmaceutically acceptable salt thereof.

30. Compound of Claim 29 wherein $R^3$ is selected from hydrido, and chloro; wherein $R^4$ is selected from chloro, methyl, tert-butyl, methylthio, trifluoromethyl, difluoromethyl, pentafluoromethyl, trifluoromethylsulfide, trifluoromethooxy, cyano, substituted or unsubstituted phenylcarbonyl, and substituted or unsubstituted phenyl; wherein $R^5$ is selected from hydrido, methyl, tert-butyl, chloro;

and wherein $R^6$ is selected from hydrido, chloro, thienyl, hydroxyiminomethyl, substituted or unsubstituted phenylethynyl, and substituted or unsubstituted phenyl; or an isomer or pharmaceutically acceptable salt thereof.

31. A compound of Formula IIc:



IIc

wherein $R^a$ is selected from hydrido and lower aralkyl; wherein $R^3$ is selected from hydrido, lower alkyl, lower hydroxyalkyl, lower alkoxy and halo; wherein $R^4$ is selected from hydrido, halo, lower alkyl, lower alkylthio, lower haloalkyl, amino, aminosulfonyl, lower alkylsulfonyl, lower alkylsulfinyl, lower alkoxyalkyl, lower alkylcarbonyl, formyl, cyano, lower haloalkylthio, substituted or unsubstituted phenylcarbonyl, lower haloalkoxy, lower alkoxy, lower aralkylcarbonyl, lower dialkylaminosulfonyl, lower alkylaminosulfonyl, lower aralkylaminosulfonyl, lower heteroaralkylaminosulfonyl, 5- or 6- membered heteroaryl, lower hydrooxyalkyl, optionally substituted phenyl and 5- or 6- membered nitrogen containing heterocyclosulfonyl; wherein $R^5$ is selected from hydrido, lower alkyl, halo, lower haloalkyl, lower alkoxy, and phenyl; and wherein $R^6$ is selected from hydrido, halo, cyano, hydrooxyiminomethyl, lower hydroxyalkyl, lower alkynyl, phenylalkynyl, lower alkyl, lower alkoxy, formyl and phenyl;

or an isomer or pharmaceutically acceptable salt thereof.

32. Compound of Claim 31 wherein $R^2$ is hydrido; wherein $R^3$ is selected from hydrido, and chloro; wherein $R^4$ is selected from chloro, methyl, tert-butyl, methylthio, trifluoromethyl, difluoromethyl, pentafluoromethyl, trifluoromethylsulfide, trifluoromethooxy, cyano, substituted or unsubstituted phenylcarbonyl, and substituted or unsubstituted phenyl; wherein $R^5$ is selected from hydrido, methyl, tert-butyl, chloro; and wherein $R^6$ is selected from hydrido, chloro, thienyl, hydroxyiminomethyl, substituted or unsubstituted phenylethynyl, and substituted or unsubstituted phenyl; or an isomer or pharmaceutically acceptable salt thereof.

33. A method of treating a cyclooxygenase-2 mediated disorder in a subject, said method comprising treating the subject having or susceptible to said disorder with a therapeutically-effective amount of a compound of Claims 1-31; or a pharmaceutically-acceptable salt thereof.

34. The method of Claim 33 wherein the cyclooxygenase-2 mediated disorder is inflammation.

35. The method of Claim 33 wherein the cyclooxygenase-2 mediated disorder is arthritis.

36. The method of Claim 33 wherein the cyclooxygenase-2 mediated disorder is pain.

37. The method of Claim 33 wherein the cyclooxygenase-2 mediated disorder is fever.

38. A pharmaceutical composition comprising a therapeutically-effective amount of a compound, said compound selected from a family of compounds of Claims 1-31; or a pharmaceutically-acceptable salt thereof.

# INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/US 98/07677

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D311/58 C07D335/06 C07D215/54 C07D311/92 C07D493/04
C07D409/04 C07D491/04 A61K31/35

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | J.BUNTING ET AL.: "KINETIC A. THERMODYNAMIC CONTROL OF PSEUDOBASE FORMAT. FROM C-3 SUBSTIT. 1-METHYLQUINOLINIUM CATIONS." CANADIAN JOURNAL OF CHEMISTRY., vol. 62, no. 7, 1984, OTTAWA CA, pages 1301-1307, XP002071264 see page 1301 - page 1305; example 6 | 1,14,15, 20 |
| A | EP 0 412 939 A (CIBA-GEIGY) 13 February 1991 cited in the application see claims | 1-31,38 |

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 13 July 1998 | 30.07.98 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Francois, J |

Form PCT/ISA/210 (second sheet) (July 1992)

# INTERNATIONAL SEARCH REPORT

Inte. ional Application No
PCT/US 98/07677

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication,where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | LOIC RENE,R.ROYER: "SUR LA SYNTHESE DE DELTA-3-CHROMENES SUBSTITUES" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY.CHIMICA THERAPEUTICA., vol. 10, no. 1, January 1975, PARIS FR, pages 72-78, XP002071265 cited in the application see page 72 - page 74; table 1 | 1-31,38 |
| A | CHEMICAL ABSTRACTS, vol. 125, no. 25, 1996 Columbus, Ohio, US; abstract no. 328458j, page 1371; column 1; XP002071266 see abstract & UKHIN,L. ET AL.: "FORMATION OF BENZOFURAN AND 2H-CHROMENES" IZV. AKAD. NAUK. SER. KHIM., vol. 5, 1996, RUSSIA, pages 1222-1228, | 1 |

1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

# INTERNATIONAL SEARCH REPORT

mational application No.
PCT/US 98/07677

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 33-37
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 33-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. ional Application No
PCT/US 98/07677

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| EP 412939 A | 13-02-1991 | AU 631913 B | 10-12-1992 |
| | | AU 6089590 A | 14-02-1991 |
| | | CA 2023016 A | 12-02-1991 |
| | | JP 3083979 A | 09-04-1991 |
| | | MX 21917 A | 28-02-1994 |
| | | PT 94912 A | 18-04-1991 |
| | | US 5155130 A | 13-10-1992 |